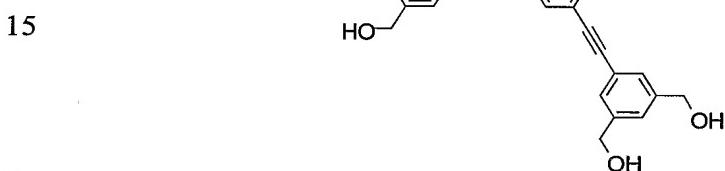
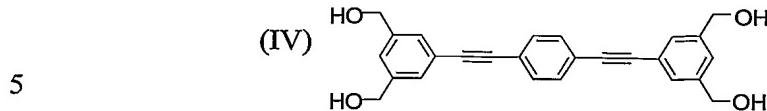
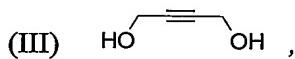


CLAIMS

WE CLAIM:

- 5 1. A composition comprising a water-soluble label comprising a 2nd generation poly(amidoamine) dendrimer encapsulating a noble metal nanocluster, wherein the label has characteristic Raman bands, expressed in wavenumbers (cm⁻¹) as a shift in energy ranging from 100-3500 cm⁻¹ from the excitation laser energy.
- 10 2. A composition comprising a water-soluble label comprising a 4th generation poly(amidoamine) dendrimer encapsulating a noble metal nanocluster, wherein the label has characteristic Raman bands, expressed in wavenumbers (cm⁻¹) as a shift in energy ranging from 100-3500 cm⁻¹ from the excitation laser energy.
- 15 3. A composition comprising a water-soluble label comprising a peptide comprising a polypeptide sequence as defined in SEQ ID NO:1 encapsulating a noble metal nanocluster, wherein the label has characteristic Raman bands, expressed in wavenumbers (cm⁻¹) as a shift in energy ranging from 100-3500 cm⁻¹ from the excitation laser energy.
- 20 4. A composition comprising a water-soluble label comprising an encapsulated noble metal nanocluster, wherein the label has a single-molecule Raman spectrum.
- 25 5. The composition of Claim 4, wherein the noble metal nanocluster comprises between 2 and 8 noble metal atoms.
- 30 6. The composition of Claim 4, wherein the noble metal is gold.
7. The composition of Claim 4, wherein the noble metal is silver.
- 35 8. The composition of Claim 4, wherein the noble metal is copper.
9. The composition of Claim 4, wherein the encapsulated noble metal nanocluster has a lifetime component of less than approximately 100 fs.
10. The composition of Claim 4, wherein the label has a single molecule anti-Stokes spectrum.

11. The composition of Claim 10, wherein the low excitation intensity is approximately 30 W/cm² at approximately 514 nm.
- 5 12. The composition of Claim 4, wherein the encapsulated noble metal nanocluster has a spectral emission that provides information about a biological state selected from the group consisting of a quantitative and qualitative presence of a biological moiety; structure, composition, and conformation of a biological moiety; localization of a biological moiety in an environment; an interaction between 10 biological moieties; an alteration in structure of a biological compound; and an alteration in a cellular process.
13. The composition of Claim 4, wherein the noble metal nanocluster has a varying charge.
- 15 14. The composition of Claim 4, wherein the size of the encapsulated noble metal nanocluster is from approximately less than 1 nm to 15 nm in diameter.
- 15 15. The composition of Claim 4, wherein the absorption cross section of the 20 encapsulated noble metal nanocluster is approximately $\sigma = 10^{-14}$ cm².
16. The composition of Claim 4, wherein the Raman cross section of the encapsulated noble metal nanocluster is approximately $\sigma = 10^{-14}$ cm².
- 25 17. The composition of Claim 4, wherein the noble metal nanocluster is encapsulated in a dendrimer.
18. The composition of Claim 17, wherein the dendrimer comprises a dendrimer core selected from the group consisting of:
- 30 (I) H₂NCD₂CD₂NH₂,
- (II)
-
- 35



19. The composition of Claim 17, wherein the dendrimer comprises poly(amidoamine).
- 20 20. The composition of Claim 19, wherein the poly(amidoamine) dendrimer is selected from the group consisting of a 0th generation, 1st generation, 2nd generation, 3rd generation, a 4th generation, and a higher generation poly(amidoamine) dendrimer.
- 25 21. The composition of Claim 19, wherein the poly(amidoamine) dendrimer is a 2nd generation, or a 4th generation OH-terminated poly(amidoamine) dendrimer.
22. The composition of Claim 4, wherein the noble metal nanocluster is encapsulated in a peptide.
- 30 23. The composition of Claim 22, wherein the peptide is approximately 5-20 amino acids in length.
- 35 24. The composition of Claim 22, wherein the peptide comprises repeating amino acid dimers.

25. The composition of Claim 24, wherein the repeating amino acid dimers are alanine and histidine.
- 5 26. The composition of Claim 22, wherein the peptide comprises a polypeptide sequence as defined in SEQ ID NO:1.
27. The composition of Claim 4, wherein the encapsulated noble metal nanocluster further comprises a functional group having a single-molecule Raman spectrum.
- 10 28. The composition of Claim 27, wherein the functional group is selected from the group consisting of C-D, C≡N, C≡C, and C≡O.
29. The composition of Claim 27, wherein the functional group has a vibrational frequency in the 1900~2300 cm⁻¹ spectral region.
- 15 30. The composition of Claim 27, where the functional group is located in any generation of a dendrimer.
- 20 31. A composition comprising a water-soluble label comprising an encapsulated noble metal nanocluster, wherein the encapsulated noble metal nanocluster has a non-linear optical property.
32. The composition of Claim 31, wherein the non-linear optical property is second harmonic generation.
- 25 33. The composition of Claim 31, wherein the noble metal nanocluster comprises between 2 and 8 noble metal atoms.
- 30 34. The composition of Claim 31, wherein the noble metal is silver.
35. The composition of Claim 31, wherein encapsulated noble metal nanocluster comprises a dendrimer encapsulated silver nanocluster.
- 35 36. The composition of Claim 35, wherein the dendrimer comprises a poly(amidoamine).

37. The composition of Claim 36, wherein the dendrimer is a 2nd generation poly(amidoamine) dendrimer.
38. The composition of Claim 35, wherein the nanocluster is excited at approximately 5 860 nm, and wherein an emission peak is observed at approximately 430 nm.
39. The composition of Claim 31, wherein the encapsulated noble metal nanocluster has a lifetime component of less than approximately 100 ps.
- 10 40. The composition of Claim 31, wherein the encapsulated noble metal nanocluster has a two-photon-excited emission at 860 nm having a shorter excited state lifetime in comparison to that resulting from single photon excitation at 430-nm.
- 15 41. The composition of Claim 31, wherein the encapsulated noble metal nanocluster has a two-photon-excited emission at 860 nm having the same excited state lifetime in comparison to that resulting from single photon excitation at 430-nm.
- 20 42. The composition of Claim 31, wherein the encapsulated noble metal nanocluster has a spectral emission that provides information about a biological state selected from the group consisting of a quantitative and qualitative presence of a biological moiety; structure, composition, and conformation of a biological moiety; localization of a biological moiety in an environment; an interaction between biological moieties; an alteration in structure of a biological compound; and an alteration in a cellular process.
- 25 43. The composition of Claim 31, wherein the size of the encapsulated noble metal nanocluster is from approximately less than 1 nm to 15 nm in diameter.
- 30 44. The composition of Claim 31, wherein a two-photon fluorescence cross section of the encapsulated noble metal nanocluster is greater than approximately 10⁵ GM.
45. A composition comprising a water-soluble fluorescent label comprising an oligonucleotide encapsulated noble metal nanocluster.
- 35 46. The composition of Claim 45, wherein the noble metal nanocluster comprises between 2 and 8 noble metal atoms.

47. The composition of Claim 45, wherein the noble metal is gold.
48. The composition of Claim 45, wherein the noble metal is silver.
5
49. The composition of Claim 45, wherein the noble metal is copper.
50. The composition of Claim 45, wherein the encapsulated noble metal nanocluster has a fluorescence quantum yield of greater than approximately 1% and has a saturation intensity ranging from approximately 1 to 10^6 W/cm².
10
51. The composition of Claim 50, wherein the low excitation intensity is approximately 30 W/cm² at approximately 460 nm.
- 15 52. The composition of Claim 45, wherein the encapsulated noble metal nanocluster exhibits a polarized spectral emission and exhibits a dipole emission pattern.
53. The composition of Claim 45, wherein the encapsulated noble metal nanocluster has a spectral emission that provides information about a biological state selected
20 from the group consisting of a quantitative and qualitative presence of a biological moiety; structure, composition, and conformation of a biological moiety; localization of a biological moiety in an environment; an interaction between biological moieties; an alteration in structure of a biological compound; and an alteration in a cellular process.
25
54. The composition of Claim 45, wherein the noble metal nanocluster has a varying charge.
55. The composition of Claim 45, wherein the size of the encapsulated noble metal
30 nanocluster is from approximately less than 1 nm to 15 nm in diameter.
56. The composition of Claim 45, wherein the noble metal nanocluster emits greater than approximately 10^8 photons before photobleaching.
- 35 57. The composition of Claim 45, wherein when the composition comprising more than one noble metal nanocluster is excited, greater than approximately 70% of the noble metal nanoclusters fluoresce for greater than approximately 10 minutes.

58. The composition of Claim 45, wherein the oligonucleotide is from approximately 1-200 nucleotides in length.
- 5 59. The composition of Claim 45, wherein the oligonucleotide is from approximately 10-35 nucleotides in length.
60. The composition of Claim 45, wherein the oligonucleotide comprises a polyA, polyG, polyT or polyC sequence.
- 10 61. The composition of Claim 45, wherein the oligonucleotide comprises a nucleotide sequence as defined in SEQ ID NO:2.
62. The composition of Claim 45, wherein the oligonucleotide comprises a nucleotide sequence as defined in SEQ ID NO:3, SEQ ID NO:4, SEQ ID NO:5, SEQ ID 15 NO:6, SEQ ID NO:7 or SEQ ID NO:8.
63. The composition of Claim 45, wherein one noble metal nanocluster binds to the oligonucleotide, and wherein the encapsulated nanocluster comprises 4 or fewer noble metal atoms.
- 20 64. A method of preparing an oligonucleotide encapsulated noble metal nanocluster capable of fluorescing, comprising the steps of:
- a) combining an oligonucleotide, an aqueous solution comprising a noble metal, and distilled water to create a combined solution;
- 25 b) adding a reducing agent;
- c) subsequently adding a sufficient amount of an acidic compound to adjust the combined solution to a neutral range pH; and
- d) mixing the pH adjusted, combined solution to allow the formation of the oligonucleotide encapsulated noble metal nanocluster.
- 30 65. The method of Claim 64, wherein the reducing agent is selected from the group consisting of light, a chemical reducing agent, a photochemical reducing agent and a combination thereof.
- 35 66. The method of Claim 64, wherein the noble metal to oligonucleotide molar ratio in step a) is approximately 0.1:1.

67. The method of Claim 64, wherein the temperature of the combined solution is between approximately 18°C to approximately 38°C from step a) through step c).
- 5 68. The method of Claim 64, wherein the temperature of the combined solution is between approximately 20°C to approximately 23°C.
69. The method of Claim 64, wherein the noble metal is selected from the group consisting of silver, gold, and copper.
- 10 70. The method of Claim 64, wherein the aqueous solution comprising a noble metal is selected from the group consisting of AgNO₃, HAuCl₄•nH₂O, and CuSO₄•nH₂O.
71. The method of Claim 64, wherein the oligonucleotide is from approximately 10-35 nucleotides in length.
- 15 72. The method of Claim 64, wherein the oligonucleotide comprises a polyA, polyG, polyT or polyC sequence.
- 20 73. The method of Claim 64, wherein the oligonucleotide comprises a nucleotide sequence as defined in SEQ ID NO:2.
74. The method of Claim 64, wherein the oligonucleotide comprises a nucleotide sequence as defined in SEQ ID NO:3, SEQ ID NO:4, SEQ ID NO:5, SEQ ID NO:6, SEQ ID NO:7 or SEQ ID NO:8.
- 25 75. The method of Claim 64, wherein the size of the oligonucleotide encapsulated noble metal nanocluster is from approximately less than 1 nm to approximately 15 nm in diameter.
- 30 76. The method of Claim 64, wherein the oligonucleotide encapsulated noble metal nanocluster is capable of fluorescing over a pH range of approximately 3 to 9.
77. The method of Claim 64, wherein the oligonucleotide encapsulated noble metal nanocluster emits greater than approximately 10⁶ photons before photobleaching.

78. The method of Claim 64, wherein when more than one oligonucleotide encapsulated noble metal nanocluster is excited, greater than approximately 70% of the noble metal nanoclusters fluoresce for greater than approximately 10 minutes at a continuous excitation energy of approximately 300 W/cm² at 514.5 nm or 476
5 nm.